ECOG Young Investigators Symposium: Winning Awards Related to NCCN Guidelines and Breast Cancer Targeting

BY JOSEPH V. SPARANO, MD, Program Committee Chair,
ECOG Young Investigator Symposium

Several noteworthy presentations were reported at the most recent Eastern Cooperative Oncology Group (ECOG) Young Investigator Symposium—the 10th annual one, including presentations from clinicians and scientists representing the disciplines of medical, surgical, and radiation oncology.

The program is intended to expose individuals early in their career to cooperative group research opportunities, and to provide them with a forum to present their research in a formal manner. Two awards were presented—one for the most outstanding presentations in the clinical research category, and one for translational research.

DR. THEJASWI POONACHA concluded that most of the guidelines are based on lower levels of evidence but with uniform expert opinion and that the results highlight the need for further research to increase the evidence base in oncology.

Clinical Research Award to Thejaswi Poonacha

The Clinical Research Award was given to Dr. Thejaswi Poonacha from Gundersen Lutheran Medical Center for his presentation, "Level of Scientific Evidence Underlying Recommendations Arising from the National Comprehensive Cancer Network Clinical Practice Guidelines." Practice guidelines play a major role in assisting physician to assimilate and apply the rapidly growing body of medical knowledge, and the NCCN guidelines are the most comprehensive, recognized, and widely used oncology standard in clinical practice. Although guidelines have expanded over the years, the level of evidence behind these guidelines has not been systematically investigated.

Dr. Poonocha and his collaborator, Dr. Ronald Go, evaluated the distribution of categories of evidence and consensus (EC) among the guidelines covering the top 10 cancers in the US—breast, prostate, lung, colorectal, melanoma, non-Hodgkin's lymphoma (NHL), kidney, pancreas, urinary bladder, and uterine — by incidence with regards to recommendations for staging, initial and salvage therapy, and surveillance practice.

The latest version of the relevant guidelines was obtained from the NCCN website. The NCCN definitions of EC include:

(1) Category I, high level of evidence with uniform consensus.

(2) Category IIA, lower level of evidence with uniform consensus.

(3) Category IIB, lower level of evidence without a uniform consensus but with no major disagreement.

(4) Category III, any level of evidence but with major disagreement.

Dr. Poonacha found that of the 1,023 recommendations for the 10 most common cancers, the proportions of Category I, IIA, IIB, and III EC were 6%, 83%, 10%, and 1%, respectively. Recommendations with Category I EC were found in kidney cancer (20%), breast cancer (19%), lung cancer (6%), pancreatic cancer (6%), NHL (6%), melanoma (6%), prostate cancer (4%), and colorectal cancer (1%) guidelines.

Urinary bladder and uterine cancer guidelines did not have any Category I recommendations. In addition, only 8% of all therapeutic recommendations were Category I.

Guidelines with the highest proportions of Category I therapeutic recommendations were for breast (30%) and kidney (28%) cancers.

No Category I recommendations were found on screening or surveillance. Dr. Poonacha concluded that most of the guidelines are based on lower level of evidence but with uniform expert opinion, and that these results highlighted the need for further research to increase the evidence base in oncology.

The results of his analysis have now been published in the *Journal of Clinical Oncology (2011;29:186-191).*

PARAIC KENNY, PHD, found *GRB7* to be a key mediator of several important phenotypes of triple-negative breast cancer cells, with the research results suggesting that *GRB7* itself, or *GRB7*-dependent pathways, may prove to be important targets for the development of specific therapies for the disease.

Translational Award to Paraic Kenny

The Translational Research Award was given to Paraic Kenny, PhD, of Albert Einstein College of Medicine for his presentation, "*GRB7* is a Key Therapeutic Target in Breast Cancer."

Triple-negative breast cancers (TNBC) lack expression of estrogen and progesterone receptors and HER2, rendering them non-responsive to the most commonly used targeted therapies in breast cancer. These tumors are typically more aggressive and more likely to metastasize to the brain than other breast cancer subtypes are, and, consequently, have a poor prognosis.

A gene expression profiling analysis of 246 TNBC patients enrolled in Trial

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Next Symposium in Florida in November

The 11th Annual ECOG Young Investigators Symposium ECOG will take place on the morning of November 12 during the next fall ECOG meeting in Hollywood, Florida. Details regarding eligibility and abstract submission procedures may be found on the *ECOG website* **(http://ecog.dfci.harvard.edu/general/yia.html)**. The abstract deadline is Friday, October 7, 2011.

View from the Other Side of the Stethoscope

The Long Goodbye

BY WENDY S. HARPHAM, MD

WENDY S. HARPHAM, MD, is an internist, cancer survivor, author, and mother of three. Her books include *Diagnosis: Cancer, After Cancer, When a Parent has Cancer*, (selected as a #1 Consumer Health Book by the *American Journal of Nursing*), *Happiness in a Storm*, and most recently, *Only 10 Seconds to Care: Help and Hope for Busy Clinicians*. She lectures on "Healthy Survivorship" issues, including recovery and late effects, raising children when a parent has cancer, clinical trials, and finding happiness in hard times. As she notes on her Web site (**www.wendyharpham.com**), her mission is to help others through the synergy of science and caring. She also writes her "On Healthy Survivorship" blog at **wendyharpham.typepad.com**

Cancer kills mothers. This truth is as startling as it is mundane. So I feel compelled to review a remarkable grief memoir by Meghan O'Rourke, a 33-year-old journalist whose mother died of cancer. In *The Long Goodbye,* her vantage offers insights about compassion in the care of *all* patients as they approach that final doctor's visit.

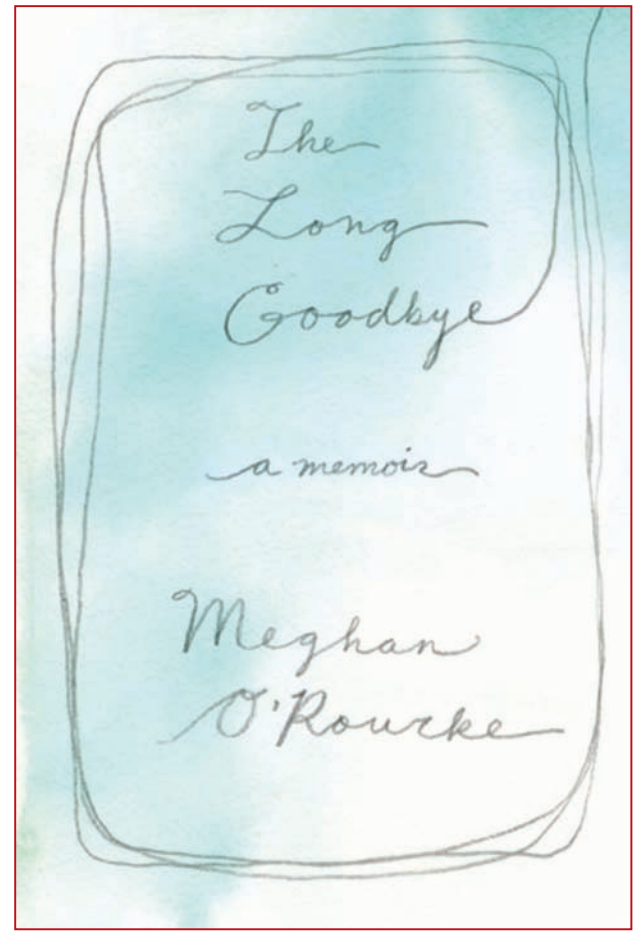
Understanding Grief

O'Rourke provides a minimalist outline of her mother's illness—diagnosis, treatment, remission, recurrence, and dying. She demonstrates her artistry by splaying the emotional chaos that defines her singular grief, while unobtrusively weaving seminal theories and schools of thought regarding mourning.

In contrast to the five stages offered by Kübler-Ross, O'Rourke asserts that grief is *"not monolithic; it's personal and variable."* Neither is it rational or linear; rather, it is a stress reaction experienced in waves and accompanied by physiological changes.

O'Rourke's experiences illustrate common psychological phenomena, such as how the death of a loved one feels sudden, even if long awaited. Mourners may become superstitious for the first time, looking for signs from the great beyond. Such seemingly irrational thoughts and feelings can disrupt the mourner's equilibrium and sense of self as a mature, sane adult, which adds to any sense of impotence and vulnerability and increases the risk of loneliness.

Importantly, intense unpleasant feelings that persist for months or longer may reflect not only the pain of separation from the deceased, but also the grief of unexpectedly losing someone else: the person the mourner got to be when the loved one was alive.



> "Sometimes it takes hearing the obvious truth from a medical authority to quash the ramblings of a tired, stressed, and grieving mind."

The Healing Power of Purpose

For people who perceive grief as the price one pays for having loved and lost, their pain can feel fruitless and punishing. To attach meaning (purpose) to this suffering is to offer a lifeline.

Analogous to pulling a rotted tooth, grief is a painful process with a purpose. Experiencing and expressing grief is how human beings integrate their great loss into everyday life so that, ultimately, they can embrace life again. In most cases, embracing life-without-this-loved-one becomes possible only after letting go—usually in fits and spurts—and accepting the loss intellectually and emotionally.

Hopeful Acceptance

Throughout survivorship, hopeful acceptance can help patients deal with uncertainty. In prior "View" columns, I've discussed some of the benefits of hopeful acceptance when treatment options are exhausted. *The Long Goodbye* opened my eyes to an additional benefit: Empowering the terminally ill to help those they will soon leave behind.

Holly Prigerson, PhD, Director of the Center for Psychosocial Oncology and Palliative Care Research at Dana-Farber Cancer Institute, explains, "When a terminally ill patient 'accepts' her death, the bereaved typically find their grief more manageable than when in 'despair.'"

That last sentence stopped me in my tracks the first time I read it. Since my diagnosis, my number one concern has been

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E2197 treated with adjuvant chemotherapy revealed that higher expression of *GRB7* was associated with tumor recurrence *(Sparano et al: JCO, Meeting Abstracts May 2009; 27:15S,500).*

GRB7 is a cytoplasmic adaptor protein that interacts with receptor tyrosine kinases, propagating information to their downstream signaling cascades. It also plays a role in integrin signaling and cell migration by binding focal adhesion kinase and ephrin receptors, and is part of the *HER2* amplicon and is frequently overexpressed in *HER2*-amplified breast tumors.

Dr. Kenny reported the results of laboratory studies in which he tested whether TNBC cell lines were dependent upon *GRB7* for proliferation, migration, and invasion. He used a highly specific cell-penetrating peptide inhibitor (G7-18NATE) and tested it on a panel of five TNBC cell lines (MDA-MB-231, MDA-MB-468, HCC1500, HCC70, and T4-2) in a series of culture assays: monolayer wound-healing assays (motility), transwell invasion assays (invasiveness), and 3D Matrigel cultures (colony growth).

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In all cases evaluated, inhibiting *GRB7* impaired the colony growth, migration, and invasion of these cell lines, induced pronounced apoptosis in TNBC cell lines and in 3D culture, but had a negligible effect on cell proliferation.

He concluded that the results implicate *GRB7* as a key mediator of several important phenotypes of TNBC breast cancer cells, and suggested that *GRB7* itself, or *GRB7*-dependent pathways, may prove to be important targets for the development of specific therapies for this disease.